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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	11

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,989	DINKINS ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *8,9,15-27,32 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10-14 and 28-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of group II, claims 1-7, 10-14 and 28-31, to the extent they read on MinD in Paper No. 10, filed 7 April 2003, is acknowledged. The traversal is on the ground(s) that Applicant believes there is a close relationship between the subject matter of the claims of groups I-V; two of the groups relate to MinE and three to MinD. Applicant urges that there would thus be no serious burden for the examiner to examine all claims.

This is not found persuasive because different nucleic acids require independent search of the sequence databases. Furthermore, the different methods have different starting products and different method steps and produce different products.

Applicant asks that at the least that groups II, IV and V be examined together, as all are drawn to the MinD gene and its use. This is not found persuasive. The different methods have different method steps and produce different products. The methods chloroplast transformation of group IV and the method for selecting chloroplast transgenics of group V would not produce the nuclear transformed plants of Group II.

The requirement is still deemed proper and is therefore made FINAL. Claims 8-9, 15-27 and 32-33 are withdrawn from consideration as being drawn to non-elected inventions. Nonelected subjected matter should be deleted from the examined claims.

2. If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the

application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Claim Objections

3. Claims 7, 13 and 31 are objected to because of the following informalities: They lack an article before "*Arabidopsis*" in line 2.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-7, 10-14 and 28-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vector encoding the *Arabidopsis* MinD protein, plants and cells transformed with it and a method of using it to produce a plant with one or few chloroplasts, does not reasonably provide enablement for vectors comprising a gene encoding a

protein with the same functional activity as the *Arabidopsis* MinD protein or encoding a derivative of the *Arabidopsis* MinD protein, plants and cells transformed with them and a method of using them to produce a plant with one or few chloroplasts. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a vector comprising a gene encoding a protein with the same functional activity as the *Arabidopsis* MinD protein or encoding a derivative of the *Arabidopsis* MinD protein, plants and cells transformed with it and a method of using it to produce a plant with one or few chloroplasts

The instant specification, however, only provides guidance for isolation of the *Arabidopsis MinD* gene by PCR using primers based on the bacterial gene sequence - the gene was already published in GenBank, (example 1); transformation of the gene into tobacco and analysis of electron transport and chloroplast morphology to show that some plants had very large chloroplasts except in guard cells (examples 1-3); Southern analysis to determine transgene number to show a correlation between abnormal chloroplast morphology and transgene number (examples 4-5); and chloroplast gene expression analysis to show that most genes were expressed normally (example 5).

The instant specification fails to provide guidance for MinD genes derived from the *Arabidopsis MinD* gene. The instant specification fails to provide guidance for exact hybridization or amplification conditions and probes/primers to use in isolation of nucleic acids other than SEQ ID NO:1.

The instant specification also fails to provide guidance for which amino acids of SEQ ID NO:1 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain MinD activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

Figure 1 of the instant specification provides an alignment between SEQ ID NO:1 and MinD proteins from *Chlorella*, *Synnechocystis* and *E. coli*. While Applicant may suggest that such an alignment can be used as guidance for making amino acid substitutions, the making of such substitutions to produce a functional protein is not predictable. Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that three presumably catalytic histidines that are maintained in the same position ADP-glucose pyrophosphorylase across 11 bacterial and plant species (abstract and pg 573, right column, paragraph 3); one would expect that an amino that is so strongly conserved would tolerate either no substitutions or only conservative substations with other basic amino acids. The substitution of one of those histidines with the conservative amino acid arginine drastically reduced enzyme activity; however, substitution with the nonconservative amino acid glutamine, had little effect on enzyme activity (see Table 1). Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Thus, amino acid substitution is unpredictable.

Furthermore, it is not clear that the *Chlorella* and *Synnechocystis* proteins are actually MinD proteins. Their identification as such was made purely on homology with the E .coli

protein after genomic sequencing (Wakasugi et al, 2001, GenBank Accession No. P56346 and Kaneko et al, 2001, GenBank Accession No. Q55900); there was no establishment of actual protein function.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids encoding derivatives of the *Arabidopsis* MinD protein. Making all possible single amino acid substitutions in an 326 amino acid long protein like that of SEQ ID NO:1 would require making and analyzing 19^{326} nucleic acids. Because nucleic acids encoding derivatives could encode proteins with many amino acid substitutions, many more than 19^{326} nucleic acids would need to be made and analyzed.

As the specification does not describe the transformation of any plant with a gene encoding a protein with the same functional activity as the *Arabidopsis* MinD protein or encoding a derivative of the *Arabidopsis* MinD protein, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with a few large chloroplasts, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

6. Claims 1-7, 10-14 and 28-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of a vector encoding a derivative of the *Arabidopsis* MinD protein, methods of its use, and cells and plants comprising it.

In contrast, the specification only describes a coding sequence from *Arabidopsis* that encodes SEQ ID NO:1. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described DNA molecules that encode a derivative of the *Arabidopsis* MinD protein within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997): at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.
> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.
> ... the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-7, 10-14 and 28-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Dependent claims are included in all rejections.

Claims 1, 5-7, 10-13 and 28-31 are indefinite in their recitation of "exogenous". It is not clear to what the gene is exogenous - the vector? *Arabidopsis*? a randomly chosen plant?

Claims 1, 10 and 28 are indefinite in their recitation of "a protein with the same functional activity as a protein encoded by the *Arabidopsis thaliana ... MinD* gene". It is unclear which protein encoded by the *MinD* gene is being referred to. Additionally, it is not clear what the exact function of the *Arabidopsis* MinD protein - what proteins does it interact with, what is its exact enzymatic activity?

Claim 3 lacks antecedent basis for the limitation "cells of Claim 2" as claim 2 is drawn to a cell.

Claims 5, 11 and 29 are indefinite in their recitation of "gene is derived from *Arabidopsis thaliana*". It is unclear what it means for a gene to be derived from a plant. Does the phrase simple mean the gene is isolated from the plant or does it mean that the gene is a derivative of the *Arabidopsis* gene? If the latter, how does it differ from the *Arabidopsis* gene?

Claims 7, 13 and 31 are indefinite in their recitation of "gene is derived from *Arabidopsis thaliana MinD* gene". It is unclear how the gene differs from the *Arabidopsis* gene. The specification, on pg 7, lines 19-25 gives a confusing definition "'derived from' a known gene or protein means that the gene or protein is the native known gene or protein, or ... is derived therefrom". The definition is confusing and meaningless because it uses the words it is defining in the definition.

Claim 28 is indefinite in its recitation of "effects" in line 5. "Effect" means to bring about or produce, and makes no sense in this claim. The word should be replaced with --affects--, which means have an effect on.

9. Claims 28-31 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The method is one of producing a transgenic plant with one or few large chloroplasts. However, the plant is simply transformed with a vector. There is no step for selecting plants with the desired phenotype. Not all transformants will have that phenotype, for example, because of position effects.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-7, 10-13 and 28-31 are rejected under 35 U.S.C. 102(a) as being anticipated by Colletti et al (2000, Curr. Biol. 10:507-516).

Colletti et al teach vectors comprising the *Arabidopsis MinD* coding sequence in the sense or antisense orientation under control of the 35S promoter and *Arabidopsis* plants whose nuclear genome is transformed with the gene (pg 508, right column, paragraph 3; pg 511, left column, paragraph 2); these plants had large chloroplasts that were reduced in number (pg 509, right column, paragraph 3; pg 511, left column, paragraph 2). Seeds of transformed plants were generated in the production of T1-T3 progeny (pg 508, right column, paragraph 3; pg 511, left column, paragraph 2). The *Arabidopsis MinD* coding sequence would be exogenous to the rest of the vector sequence.

12. Claims 1-7, 10-13 and 28-31 are rejected under 35 U.S.C. 102(a) as being anticipated by Kanamaru et al (2000, Plant Cell Physiol. 41:1119-1128 and GenBank Accession No. AB030278, December 2000).

Kanamaru et al teach a vector comprising the *Arabidopsis MinD* gene (GenBank Accession No. AB030278) under control of the 35S promoter and *Arabidopsis* plants whose nuclear genome is transformed with the gene; these plants had large chloroplasts that were reduced in number (Figure 6). Seeds of transformed plants were generated in the production of T2 and T3 progeny (pg 1121, left column, paragraph 2). The *Arabidopsis MinD* coding sequence would be exogenous to the rest of the vector sequence.

13. Claims 1-2 and 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Huang et al (1996, J. Bacteriol. 178:5080-5085).

It is noted that the vector of claim 1 comprises a gene that if it were expressed in a plant cell would alter chloroplast size and number; the claim does not require that the vector be one that has plant expression components, nor does it require that the gene be from a plant. Also this rejection is made in keeping with the 112, 2nd rejections above.

Huang et al teach expression vectors encoding a bacterial MinD protein and yeast cells comprising the vector; the bacterial protein would have the same function as the *Arabidopsis* MinD protein (pg 5083, left column, paragraph . Furthermore, the bacterial gene would be a derivative of the *Arabidopsis MinD* gene and the gene would be exogenous to yeast.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
June 11, 2003